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FLT3 inhibitors potentially improve response rates in acute myeloid leukemia harboring t(6;9)(*DEK::NUP214*): The Mayo Clinic experience

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FLT3 inhibitors potentially improve response rates in acute myeloid leukemia harboring t(6;9)(*DEK::NUP214*): The Mayo Clinic experience

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CMC collected data, performed the analyses, drafted the manuscript, and collaboratively designed the study. ANS, PTG, and AA assisted with data collection. SHK and AA collaboratively designed and oversaw the study. All co-authors provided patient care, assisted with data collection, and critically reviewed the manuscript. All authors approved the final draft.

Conflicts of Interest
The authors declare no conflicts of interest with this work.

Data Sharing
Original data will be provided to collaborating investigators upon reasonable request to the corresponding authors after requisite institution review board approval.

TO THE EDITOR:

Translocation (6;9)(p23;q34.1) is detected in 1% of acute myeloid leukemia (AML) cases and is considered a high-risk subtype by European Leukemia Network (ELN) 2022 criteria.[1] Compared to AML overall, t(6;9) AML affects younger adults with a median age of 35 – 38 years at diagnosis, and is historically associated with poor overall survival (OS) of roughly 14 months.[2,3] Most cases (62 – 88%) harbor internal tandem duplications of fms-like tyrosine kinase 3 (*FLT3*-ITD).[2-6] While preliminary data suggest that FLT3 inhibitors (FLT3i) might provide benefit[7,8], this has not yet been confirmed in larger studies. Although outcomes have improved with allogeneic hematopoietic cell transplantation (alloHCT),[6,9,10] survival remains dismal for patients ineligible for transplant.[3] This report describes a three-site experience with t(6;9) AML at an academic tertiary care center with a large HCT referral program.

After institutional review board approval, all patients with t(6;9)(p23;q34.1) AML seen across the three Mayo Clinic sites in the US between 2010 – 2023 were identified via retrospective chart review; this included eight previously-published patients.[11] A separate AML cohort excluding t(6;9) was curated pragmatically over a similar timeframe. Data from the time of diagnosis or presentation to Mayo Clinic were abstracted. Mutation assessment was performed as described.[12] When necessary, *FLT3* allelic ratio was estimated from the variant allele fraction (VAF).[12,13] Classification and response were assessed by ELN 2022 criteria.[1] Measurable residual disease (MRD) was assessed by t(6;9)(p23;q34.1) specific fluorescence *in situ* hybridization (FISH) of ≥500 nuclei (sensitivity 0.6%) or multiparametric flow cytometry (MFC; sensitivity 0.01%). Categorical variables were compared by Fisher exact or Pearson χ^2 tests and continuous variables by Mann-Whitney U tests or two-way ANOVA with Tukey correction. Univariate and multivariate analyses utilized Cox proportional hazards models. Survival was assessed via the Kaplan-Meier method with log-rank comparisons. Calculations were performed with BlueSky Statistics (v10.3.1) or GraphPad Prism (v.10.1.2). P <0.05 was considered significant.

Twenty-one patients (12 females, 57%) with t(6;9) AML were identified with median age 39 years (**Table 1**). Anemia was common (n=19, 90%) and thrombocytopenia was universal. Peripheral blasts were identified in 19 (90%) patients. Cytogenetic analyses identified isolated t(6;9)(p23;q34.1) in 8 (40%) cases, whereas 3 (15%) exhibited a complex karyotype. Most cases (n=14, 70%) harbored *FLT3*-ITD mutations (median VAF 39%), which were the sole mutations identified in all 14 cases that harbored them (**Figure S1A-B**). No *FLT3* tyrosine kinase domain mutations were detected.

Most (n=19, 90%) received frontline induction therapy with cytarabine plus an anthracycline (**Table S1**). Six of 14 (43%) patients harboring *FLT3*-ITD received a FLT3i during induction. Four (29%) additional patients received a FLT3i with consolidation or salvage therapy. Following induction, 12 of 19 (63%) evaluable patients achieved a compete response (CR) or CR with either partial (CRh) or incomplete (CRi) hematologic recovery. An additional 5 patients achieved CR/CRh/CRi after salvage or consolidative chemotherapy (**Table 1**). All *FLT3* wild-type (WT) cases eventually achieved a CR/CRh/CRi for an overall response rate (ORR) of 100%. Amongst *FLT3*-ITD cases, the ORR was 77%. Sixteen patients (76%) proceeded to alloHCT.

The role of MRD assessment in adverse-risk AML is not well defined.[14] Because methodology has evolved over time, the present analysis considered MRD based on MFC (n=4) or FISH (n=11) testing within 60 days of induction, prior to transplant, or at post-transplant day +100 (**Figure S1C**). After induction, only 2 of 11 (18%) patients achieving morphologic CR had undetectable MRD. Ten of 11 (91%) evaluable patients were MRD-negative prior to alloHCT. All evaluable patients were MRD-negative at post-transplant day +100. Of the four patients with MRD testing strictly by MFC, all were MRD-negative prior to HCT, and the three evaluable cases remained MRD-negative on day +100 (**Figure S1D**). When both MFC and FISH were performed, all results were concordant.

Eight patients (38%) were deceased at last follow up. With median follow up of 72 months, the 2-year OS of the cohort was 71% while the median OS (mOS) was not reached (NR; **Figure 1A**).

The mOS was NR irrespective of *FLT3* status (p=0.45; **Figure 1B**). Amongst *FLT3*-ITD cases, OS was numerically longer (NR vs 24 months, p=0.17; **Figure 1C**) and there were fewer deaths (1 vs 5) amongst those who received a FLT3i during induction (**Table 2**). Accordingly, the 2-year OS was numerically higher for those receiving a FLT3i with induction (83% vs 50%). Although statistically insignificant, these trends again suggest that FLT3is benefit a subgroup of patients.

AlloHCT significantly prolonged survival compared to those who were not transplanted (mOS NR vs 19 months, p=0.0001; **Figure 1D**). Two-year survival rates were also superior with alloHCT (88% vs 20%; **Table 2**). Moreover, alloHCT was beneficial irrespective of *FLT3* status (p<0.03 for both comparisons; **Figure 1E-F**). There was no difference in survival when patients were stratified by myeloablative vs non-myeloablative conditioning intensity (p=0.55) or conditioning regimen (p=0.40). Transplant related mortality (TRM) was 6%, as one patient expired on post-HCT day +32 from sinusoidal obstruction syndrome.

Analogous results were obtained when patients with complex cytogenetics (n=3) were excluded, with mOS of 81 months and 2-year OS of 65% for the remaining patients. There was again no difference in mOS when stratified by *FLT3* status (p=0.21). AlloHCT similarly improved mOS (NR vs 19 months, p=0.0014), with 2-year OS of 83% vs 20% for those who did and did not undergo HCT, respectively.

There was no difference in OS based on MRD status after induction (p=0.64) or prior to alloHCT (p=0.75; **Figure S1E-F**). When stratified by MRD-negativity at any time prior to HCT (if transplanted), there was a trend toward improved survival compared to MRD-positive patients (mOS NR vs 29 months, p=0.069; **Figure S1G**). Accordingly, the 2-year survival was higher (90% vs 60%) with fewer deaths (1 vs 3) amongst MRD-negative patients compared to positive patients (**Table 2**). However, these analyses are confounded, as all patients who achieved MRD-negativity proceeded to alloHCT. Amongst the four patients with MRD testing by MFC, the mOS was NR with 2-year OS of 75% (**Figure S1H**).

Survival of the t(6;9) AML cohort was better than anticipated; therefore, these outcomes were compared to those from a separate non-t(6;9) AML cohort (n=160; **Table S2**). Patients were classified as ELN favorable (n=17, 11%), intermediate (n=61, 38%), or adverse (n=82, 51%) risk.[1] At last follow up, 47 (29%) patients had undergone alloHCT and 114 (71%) had died. With

median follow up of 87 months, the mOS was 19 months (95% CI 15 – 28) with 2-year OS of 44%. Across the three ELN risk categories, the mOS was 62, 26, and 9 months with 2-year OS of 69%, 53%, and 31%, respectively (**Figure 1G**). AlloHCT provided a significant survival benefit in the intermediate and adverse-risk groups (each $p<0.0001$) but not in the favorable-risk group ($p=0.39$), as expected for favorable-risk disease.[15]

Surprisingly, patients with t(6;9) AML fared better than the ELN adverse-risk comparison group (**Figure 1G**). Rather, the mOS of t(6;9) patients approximated that of the favorable-risk group (NR vs 62 months, $p=0.51$) with 2-year OS of 71% vs 69%, respectively. However, patients with t(6;9) AML benefitted from alloHCT whereas those with favorable-risk disease in the comparison cohort did not. Indeed, t(6;9) AML patients who received alloHCT fared similarly to transplanted intermediate-risk patients, with 2-year OS of 88% and 87%, respectively ($p=0.32$; **Figure 1H**). Survival was also similar between t(6;9) and non-t(6;9) patients of comparable age (**Figure 1I**). These data raise the question as to whether t(6;9) AML should be reclassified as intermediate-risk, particularly for those treated with FLT3i and alloHCT. Notably, the 2022 ELN classification schema now categorizes AML with *FLT3*-ITD (without adverse-risk genetic lesions) in the intermediate-risk group.[1]

Attempts were made to identify parameters associated with OS. Univariate Cox regression identified MCV ($p=0.045$) and the peripheral blood blast percentage ($p=0.011$) as adverse prognostic factors while receipt of alloHCT was beneficial ($p=0.0024$). Neither *FLT3* status, induction FLT3i use, nor best MRD status correlated with OS. In the multivariate model of significant factors, only alloHCT retained significance (hazard ratio 0.11, 95% CI 0.02 – 0.68, $p=0.017$).

Due to the rarity of t(6;9) AML, this study was underpowered to determine whether FLT3i or MRD-negativity truly improve survival. Moreover, because this dataset spans an era of evolving MRD assessment standards and few patients had MRD testing by contemporary methods, larger combined analyses are needed to establish the role of frontline FLT3i and MRD monitoring in this setting. Furthermore, the mOS of this cohort (NR) is longer than previously reported (14 – 27 months)[2,3,6], likely signifying transplant referral bias, as alloHCT improves outcomes in t(6;9) AML.[6,9-11] Within these limitations, alloHCT significantly improved mOS in this cohort irrespective of *FLT3* or MRD status, and multivariate analysis identified alloHCT as the only prognostic factor.

In conclusion, t(6;9) AML has poor OS in the absence of alloHCT, and all eligible patients should be considered for transplant in first remission irrespective of MRD status. Although a definitive benefit has yet to be proven, FLT3i are an enticing avenue to improve response rates in *FLT3*-ITD positive cases. Collectively, these interventions may provide sufficient benefit to reclassify t(6;9) AML as an intermediate-risk disease and need to be validated in larger studies.

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Table 1. Patient Demographics

Metric	Evaluable Cases (n)	Result
Demographics		
Age at diagnosis, years	21	39 (15 - 67)
Male	21	9 (43%)
Female	21	12 (57%)
Laboratory Parameters		
Hemoglobin, g/dL	21	8.6 (5.8 – 13.0)
Mean corpuscular volume, fL	20	98.6 (82.7 – 110.1)
Platelet count, $x10^9$/L	21	42 (18 – 89)
White blood cell count, $x10^9$/L	21	9.7 (0.5 – 99.5)
Absolute neutrophil count, $x10^9$/L	20	1.73 (0.12 – 16.73)
Peripheral blood blasts, %	21	20 (0 – 89)
Bone marrow blasts, %	19	63 (7 – 90)
Cytogenetic Parameters		
DEK::NUP214 FISH nuclei, %	14	78.1 (24.8 – 98.2)
Isolated t(6;9)(p23;q34.1)	20	8 (40%)
Complex karyotype	20	3 (15%)
Mutation Status		
Number of mutations	21	1 (0 – 2)
FLT3-ITD	20	14 (70%)
FLT3-ITD allelic ratio	14	0.5 (0.05 – 7.3)
FLT3-ITD variant allele fraction, %	14	39 (10 – 88)
Treatment		
Anthracycline-based induction in first line	21	19 (90%)
Azacitidine plus venetoclax in first line	21	1 (5%)
Received a FLT3i with induction[1]	14	6 (43%)
Received a FLT3i in later lines only[2]	14	4 (29%)
Allogeneic HCT Parameters		
Underwent allogeneic HCT	21	16 (76%)
Myeloablative conditioning	16	13 (81%)
Busulfan and cyclophosphamide conditioning	16	5 (31%)
Busulfan and fludarabine conditioning	16	5 (31%)
Matched related donor	16	5 (31%)
Matched unrelated donor	16	6 (38%)
Mobilized peripheral blood stem cell source	16	14 (88%)
Response		
Achieved CR, CRh, or CRi after induction	19	12 (63%)
Achieved CR, CRh, or CRi at any time	20	17 (85%)
Lines of therapy to first CR, CRh, or CRi	17	1 (1 – 3)
Total lines of therapy received	20	3 (1 – 8)
Outcomes		
Deceased	21	8 (38%)
Transplant related mortality	16	1 (6%)

Data are presented as either median (range) or n (%), as applicable. [1]Patients who received a FLT3 inhibitor (FLT3i) with induction therapy may have also received a FLT3i during consolidation or in later lines of therapy (Supplemental Table 1). [2]Indicates patients with a FLT3 mutation who did not receive a FLT3i with induction therapy, but subsequently received one during either consolidation or salvage. Abbreviations: FISH, fluorescence in situ hybridization; *FLT3*-ITD, fms-like tyrosine kinase 3 internal tandem duplications; HCT, hematopoietic cell

transplantation; CR, complete response; CRh, complete response with partial hematologic recovery; CRi, complete response with incomplete hematologic recovery.

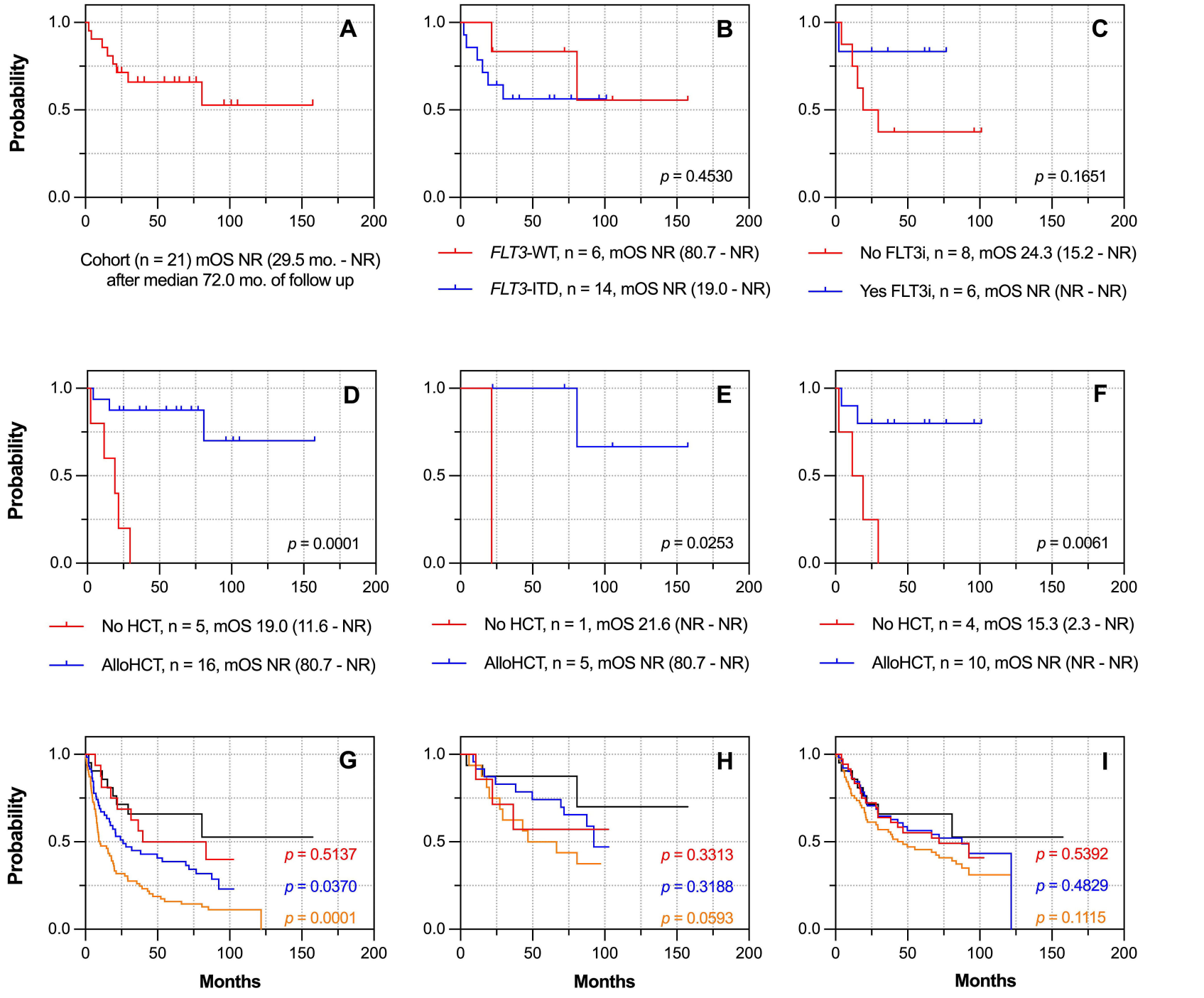
Table 2. Treatment Responses and Survival Outcomes

	ORR (%)[a]	MRD- (%)[b]	Deceased (%)	2-Year OS (%)	mOS (mo.)	*P*[c]
Cohort	85%	56%	38%	71%	NR	
***FLT3*-ITD Status**						
Negative	100%	50%	33%	83%	NR	0.4530
Positive	77%	58%	43%	64%	NR	
Induction FLT3i	83%	83%	17%	83%	NR	0.1651
No induction FLT3i	71%	33%	63%	50%	24	
Allogeneic HCT						
Received HCT	100%	77%	19%	88%	NR	0.0001
No HCT	40%	0%	100%	20%	19	
MRD Status[d]						
Negative	N/A	N/A	10%	90%	NR	0.0688
Positive	N/A	N/A	60%	60%	29	

Percentage denominators are based on the number of evaluable patients for the specified metric. [a]The ORR includes patients with CR, CRh, and CRi. ORR and MRD status are presented as the best response attained. For patients who underwent allogeneic HCT, these data represent the best response achieved prior to HCT, as all patients who underwent HCT and were subsequently evaluable achieved a CR_{MRD-} status thereafter. MRD was assessed by MFC or FISH as described in the text. [b]The denominator for MRD negative percentages include both patients with MRD and persistent disease. [c]P values are for median OS comparisons. [d]These rows consider only patients who achieved morphologic remission and were evaluable for MRD status.

Abbreviations: CR, complete response; CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; FISH, fluorescence in situ hybridization; *FLT3*-ITD, fms-like tyrosine kinase 3 internal tandem duplications; HCT, hematopoietic cell transplantation; MFC, multiparametric flow cytometry; mo, months; MRD, measurable residual disease; N/A, not applicable; NR, not reached; ORR, overall response rate; OS, overall survival.

Figure 1. Overall Survival in t(6;9)(*DEK::NUP214*) AML and Compared to ELN Risk Groups. (A) The median overall survival (mOS) of the entire cohort. **(B-F)** mOS of *FLT3* wild type vs. *FLT3*-ITD cases (B); *FLT3*-ITD positive cases receiving a FLT3i vs. those that did not (C); t(6;9) AML patients undergoing allogeneic hematopoietic cell transplantation (alloHCT) vs. those who did not (D); cases with wild type *FLT3* who underwent alloHCT vs. those who did not (E); and those with a *FLT3*-ITD mutation who underwent alloHCT compared to those who did not (F). **(G)** Comparison of OS in the t(6;9) AML cohort vs. the ELN favorable, intermediate, and adverse-risk groups. **(H)** Comparison of OS in the t(6;9) AML subset who underwent alloHCT vs. the ELN favorable, intermediate, and adverse-risk groups who also underwent alloHCT. (I) Comparison of OS in the t(6;9) AML cohort vs age-restricted subgroups of the comparison cohort; the median (range) ages of the three subgroups are 38 (18 – 55), 50 (18 – 60), and 56 (18 – 65) years, respectively. In G-I, *p* values depict the comparison between the t(6;9) AML cohort and the color-matched subgroup of the comparison cohort. All survival times are denoted as median (95% confidence interval) in months (mo).


A
B
C
D
E
F
G
H
I
Probability
Months
Cohort (n = 21) mOS NR (29.5 mo. - NR)
after median 72.0 mo. of follow up
p = 0.4530
p = 0.1651
FLT3-WT, n = 6, mOS NR (80.7 - NR)
FLT3-ITD, n = 14, mOS NR (19.0 - NR)
No FLT3i, n = 8, mOS 24.3 (15.2 - NR)
Yes FLT3i, n = 6, mOS NR (NR - NR)
p = 0.0001
p = 0.0253
p = 0.0061
No HCT, n = 5, mOS 19.0 (11.6 - NR)
AlloHCT, n = 16, mOS NR (80.7 - NR)
No HCT, n = 1, mOS 21.6 (NR - NR)
AlloHCT, n = 5, mOS NR (80.7 - NR)
No HCT, n = 4, mOS 15.3 (2.3 - NR)
AlloHCT, n = 10, mOS NR (NR - NR)
p = 0.5137
p = 0.0370
p = 0.0001
p = 0.3313
p = 0.3188
p = 0.0593
p = 0.5392
p = 0.4829
p = 0.1115
t(6;9) AML, n = 21, mOS NR (29.5 - NR)
Favorable, n = 17, mOS 61.6 (22.0 - NR)
Intermediate, n = 61, mOS 26.0 (16.6 - 76.8)
Adverse, n = 82, mOS 9.3 (8.1 - 19.1)
t(6;9) AML, n = 16, mOS NR (80.7 - NR)
Favorable, n = 7, mOS NR (22.0 - NR)
Intermediate, n = 24, mOS 92.4 (71.7 - NR)
Adverse, n = 16, mOS 56.7 (27.2 - NR)
t(6;9) AML, n = 21, mOS NR (29.5 - NR)
Age ≤ 55 y, n = 37, mOS 71.7 (29.4 - NR)
Age ≤ 60 y, n = 53, mOS 87.6 (43.0 - NR)
Age ≤ 65 y, n = 80, mOS 46.7 (28.1 - 87.6)

Supplemental Data for:

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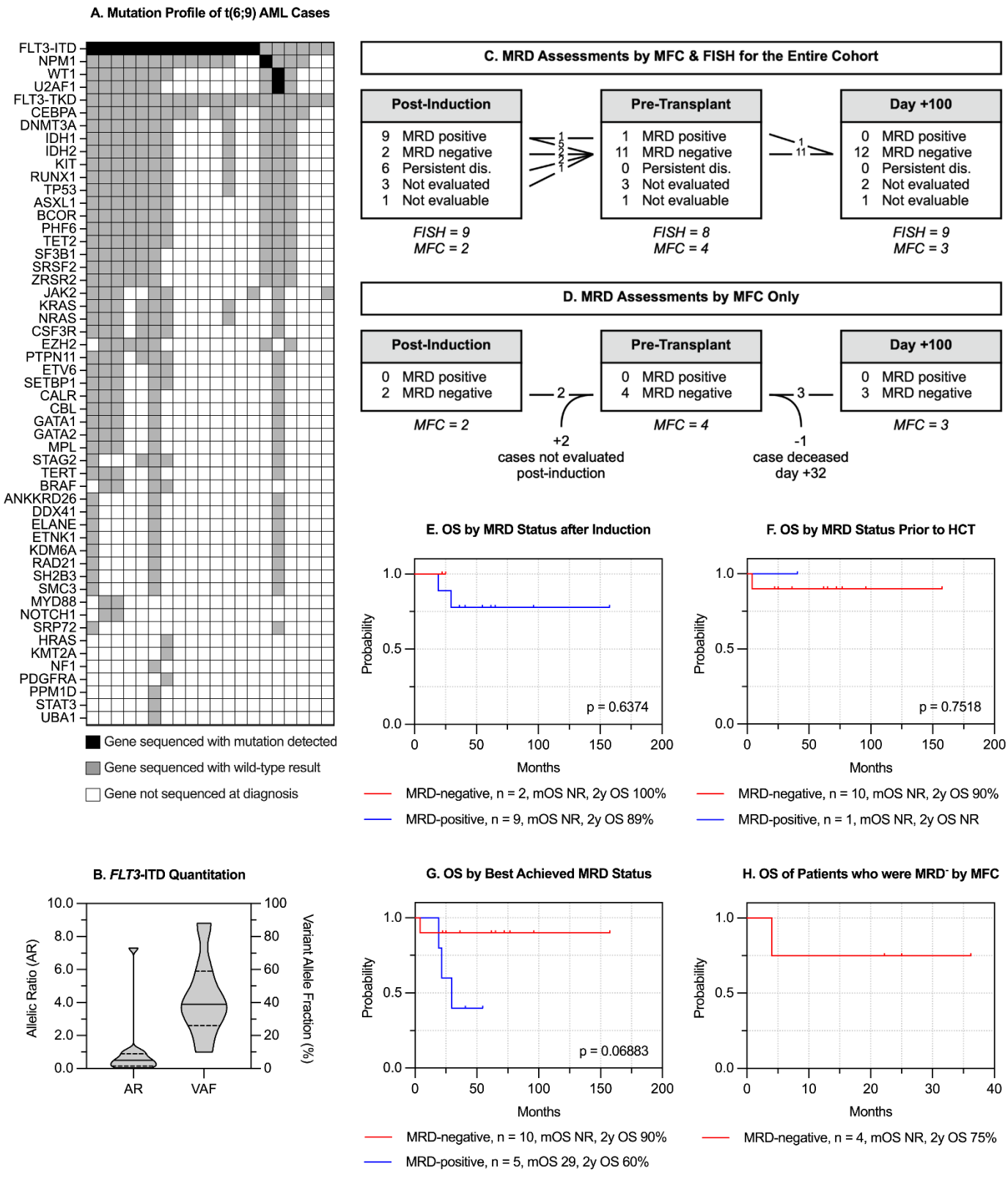

Figure 1. Mutation Profile and MRD Assessment of Evaluable Cases of t(6;9) AML. (A) Of the 21 patients identified retrospectively, 20 had evaluable mutation sequencing at the time of diagnosis or referral. Each column depicts a single case. Black cells represent detected mutations, gray cells represent sequenced genes with wild type results, and white cells represent genes for which sequencing data from the time of diagnosis were unavailable. The number (frequency) of detected mutations was 14 (70%) for *FLT3*-ITD, 1 (6%) for *NPM1*, 1

(11%) for *U2AF1*, and 1 for (10%) *WT1*. **(B)** Of n = 13 evaluable cases, the median *FLT3*-ITD allelic ratio was 0.5 (range 0.05 – 7.3) at the time of diagnosis or presentation. Of n = 7 cases where next generation sequencing (NGS) was available, the median *FLT3*-ITD variant allele fraction (VAF) was 39% (range 10 – 88%). In both violin plots, the solid bars depict the median while dashed bars depict the upper and lower quartiles. **(C)** MRD was assessed by either multiparameter flow cytometry (MFC) or fluorescence *in situ* hybridization (FISH) of at least 500 nuclei at three time points: within 60 days of induction, prior to allogeneic hematopoietic cell transplantation (alloHCT), or on post-HCT day +100. **(D)** The small group (n = 4) of patients whose MRD status was assessed by contemporary methods only (i.e., MFC). Kaplan-Meier plots depict the median OS (mOS) of patients stratified by MRD status **(E)** after induction therapy, **(F)** prior to alloHCT, **(G)** the best MRD status achieved at any time, or **(H)** as assessed by contemporary MFC. In most subgroups, mOS was not reached (NR); otherwise, mOS is depicted in months. No survival comparisons are statistically significant.

Table S1. Overview of t(6;9) AML Patient Treatment and Outcomes by Case

Age / Gender	Sequential Lines of Treatment	HCT Parameters	Best Response	Status at Last Follow Up	Cause of Death
46 F	Cytarabine + idarubicin HiDAC consolidation Allogeneic HCT	MRD Bu/Cy PBSCT	CR	Deceased	Mesenteric thrombosis with bowel necrosis
19 F	Cytarabine + daunorubicin + midostaurin HiDAC + midostaurin consolidation Allogeneic HCT	Haplo Flu/Bu/Thiotepa PBSCT	CR	Alive	
42 M	Cytarabine + daunorubicin HiDAC consolidation Allogeneic HCT	MRD Bu/Cy BMT	CR	Alive	
67 M	Venetoclax + azacitidine + gilteritinib		NR	Deceased	r/r AML
42 M	Cytarabine + daunorubicin + midostaurin HiDAC + midostaurin Allogeneic HCT	MRD Bu/Flu PBSCT	CR	Alive	
20 F	Cytarabine + idarubicin (7+3) x2 HiDAC consolidation Allogeneic HCT	mMUD Flu/Cy/TBI DUCBT	CR	Alive	
27 F	Cytarabine + idarubicin x2 MEC salvage FLT3i trial (AC220) Azacitidine Decitabine + sorafenib Quizartinib Crenolanib Hydroxyurea		NR	Deceased	r/r AML
32 F	Cytarabine + daunorubicin x2 Allogeneic HCT	MUD Bu/Cy PBSCT	CR	Alive	
54 F	Cytarabine + daunorubicin + midostaurin HiDAC + midostaurin consolidation Allogeneic HCT	MUD Bu/Flu PBSCT	CR	Alive	
39 M	Cytarabine + idarubicin HiDAC consolidation Allogeneic HCT CLAG-M	MRD Bu/Flu PBSCT		Deceased	r/r AML
57 M	Azacitidine Cytarabine + idarubicin HiDAC consolidation FLT3i trial (AC220)		CRh	Deceased	r/r AML
52 F	Cytarabine + idarubicin HiDAC consolidation Allogeneic HCT	MUD Bu/Cy PBSCT	CR	Alive	

60 F	Cytarabine + idarubicin CLAG-M salvage HiDAC consolidation Anti-CD47 antibody trial (TT1-621)		CRi	Deceased	r/r AML
63 M	Cytarabine + daunorubicin HiDAC consolidation Allogeneic HCT	MUD Flu/Mel PBSCT	CR	Alive	
41 F	Cytarabine + anthracycline x2 CLAG-M salvage Allogeneic HCT	MUD Flu/Mel PBSCT	CR	Alive	
29 M	Cytarabine + idarubicin HiDAC salvage HiDAC consolidation Allogeneic HCT	MUD Bu/Flu PBSCT	CR	Alive	
39 M	Cytarabine + idarubicin MEC salvage Allogeneic HCT	Haplo Bu/Flu PBSCT	CR	Alive	
36 F	Cytarabine + daunorubicin + midostaurin HiDAC consolidation Allogeneic HCT	MUD Bu/Cy PBSCT	CR	Alive	
23 M	Cytarabine + idarubicin + etoposide ADE + midostaurin consolidation Allogeneic HCT	Haplo Flu/TBI PBSCT	CRh	Deceased	Post-transplant SOS with multiorgan failure (deceased day +32)
19 F	Cytarabine + daunorubicin + midostaurin + GO HiDAC + midostaurin consolidation Allogeneic HCT Gilteritinib maintenance	Haplo Flu/TBI PBSCT	CR	Alive	
16 F	Cytarabine + idarubicin Venetoclax + azacitidine FLAG-Ida Decitabine + vorinostat-FLAG Venetoclax + gilteritinib + daratumumab Mitoxantrone + etoposide + GO Vyxeos + decitabine + vorinostat Imatinib + sirolimus		NR	Deceased	r/r AML

Abbreviations not defined elsewhere: F, female; M, male; ADE, cytarabine, daunorubicin, and etoposide; CLAG-M, cladribine, cytarabine, granulocyte colony stimulating factor (G-CSF), and mitoxantrone; FLAG-Ida, fludarabine, cytarabine, G-CSF, and idarubicin; GO, gemtuzumab ozogamicin; HiDAC, high-dose cytarabine; MEC, mitoxantrone, etoposide, and cytarabine; MUD, matched unrelated donor; MRD, matched related donor; mMUD, mismatched unrelated donor; Haplo, haploidentical donor; Bu, busulfan; Cy, cyclophosphamide; Flu, fludarabine; Mel, melphalan; TBI, total body irradiation; BMT, bone marrow harvest transplantation; DUCBT, double umbilical cord blood transplantation; PBSCT, peripheral blood stem cell transplantation; NR, no response; r/r, relapsed/refractory; SOS, sinusoidal obstruction syndrome.

Table S2. Demographics of the Comparison Cohort.

Characteristic	Non-t(6;9) Cohort	ELN Favorable	ELN Intermediate	ELN Adverse
n	160	17	61	82
Demographics				
Age, years	65 (18 – 86)	59 (19 – 78)	63 (19 – 86)	68 (18 – 86)
Male	87 (54%)	7 (41%)	28 (46%)	52 (63%)
Female	73 (46%)	10 (59%)	33 (54%)	30 (37%)
Cytogenetics				
Normal karyotype	92 (58%)	11 (65%)	46 (75%)	35 (43%)
Complex karyotype	23 (14%)	0 (0%)	0 (0%)	23 (28%)
Mutations				
Number of mutated genes	2 (0 – 7)	3 (0 – 5)	2 (0 – 6)	3 (0 – 7)
ASXL1	27 (17%)	1 (6%)	4 (7%)	22 (27%)
BCOR	11 (7%)	0 (0%)	2 (3%)	9 (11%)
CALR	1 (1%)	0 (0%)	0 (0%)	1 (1%)
CBL	4 (3%)	0 (0%)	2 (3%)	2 (2%)
CEBPA	8 (5%)	1 (6%)	2 (3%)	5 (6%)
CSF3R	2 (1%)	0 (0%)	1 (2%)	1 (1%)
DNMT3A	38 (24%)	4 (24%)	18 (30%)	16 (20%)
EZH2	6 (4%)	0 (0%)	0 (0%)	6 (7%)
FLT3 (Any)	28 (18%)	5 (29%)	17 (28%)	6 (7%)
FLT3-ITD	23 (14%)	2 (12%)	16 (26%)	5 (6%)
FLT3-TKD	6 (4%)	3 (18%)	1 (2%)	2 (2%)
GATA2	5 (3%)	0 (0%)	2 (3%)	3 (4%)
IDH1	8 (5%)	1 (6%)	4 (7%)	3 (4%)
IDH2	26 (16%)	4 (24%)	9 (15%)	13 (16%)
JAK2	9 (6%)	0 (0%)	1 (2%)	8 (10%)
KIT	6 (4%)	1 (6%)	4 (7%)	1 (1%)
KRAS	6 (4%)	2 (12%)	1 (2%)	3 (4%)
MPL	2 (1%)	0 (0%)	1 (2%)	1 (1%)
NOTCH1	1 (1%)	0 (0%)	1 (2%)	0 (0%)
NPM1	19 (12%)	12 (71%)	6 (10%)	1 (1%)
NRAS	15 (9%)	3 (18%)	6 (10%)	6 (7%)
PHF6	5 (3%)	0 (0%)	2 (3%)	3 (4%)
PTPN11	5 (3%)	2 (12%)	2 (3%)	1 (1%)
RUNX1	29 (18%)	0 (0%)	5 (8%)	24 (29%)
SETBP1	4 (3%)	0 (0%)	1 (2%)	3 (4%)
SF3B1	7 (4%)	0 (0%)	0 (0%)	7 (9%)
SRSF2	23 (14%)	2 (12%)	7 (11%)	13 (16%)
TET2	31 (19%)	3 (18%)	14 (23%)	14 (17%)
TP53	29 (18%)	0 (0%)	0 (0%)	29 (35%)
U2AF1	15 (9%)	1 (6%)	3 (5%)	11 (13%)
WT1	20 (13%)	6 (35%)	6 (10%)	8 (10%)
ZRSR2	1 (1%)	0 (0%)	0 (0%)	1 (1%)
Outcomes				
Allogeneic HCT	47 (29%)	7 (41%)	24 (39%)	16 (20%)
Death	114 (71%)	9 (53%)	38 (62%)	67 (82%)

Data are presented as median (range) or n (%), as appropriate. Abbreviations and units are as defined in the main text.